

Claims

1. A method for generating a transgenic nematode expressing at least one mammalian GPCR in a sensory neuron linked to behavior, wherein said method comprises the following steps:

- (a) preparing at least one gene expression construct comprising a nucleotide sequence encoding a mammalian GPCR operably linked to a promotor specific for sensory neurons;
- (b) generating a transgenic nematode by introducing the said at least one gene expression construct into the nematode; and
- (c) examining if the resulting nematode is a transgenic nematode expressing the at least one mammalian GPCR.

2. The method according to claim 1, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal GPCR.

3. The method according to claim 1, wherein the promotor specific for a sensory neuron is selected from the group comprising *daf-7*, *flp-6*, *gpa-2*, *gpa-4*, *gpa-11*, *gcy-5*, *gcy-6*, *gcy-7*, *gcy-8*, *nhr-38*, *nhr-79*, *odr-7*, *odr-10*, *ops-1*, *str-1*, *str-2*, *str-3*, *sra-7*, *sra-9*, *srg-2*, and *srg-8*.

4. The method according to claim 1, wherein the nematode belongs to the subgenus *Caenorhabditis*.

5. The method according to claim 4, wherein the nematode is *Caenorhabditis elegans*.

6. The method according to claim 1, wherein it is further determined whether the transgenic nematode shows a different behavioral phenotype selected from the group comprising chemoattraction towards or chemorepulsion from a substance as compared to wild-type nematodes.

7. A method for generating a transgenic nematode expressing at least one mammalian GPCR in a sensory neuron linked to behavior, wherein said method comprises the following steps:

- (a) preparing at least one gene expression construct comprising a nucleotide sequence encoding a mammalian GPCR operably linked to a promotor specific for sensory neurons and a further gene expression construct comprising a nucleotide sequence encoding an accessory protein operably linked to a promotor specific for sensory neurons;
- (b) generating a transgenic nematode by introducing the at least one gene expression construct encoding a mammalian GPCR and the gene expression construct encoding an accessory protein into the nematode; and
- (c) examining if the resulting nematode is a transgenic nematode co-expressing the at least one mammalian GPCR and the accessory protein.

8. The method according to claim 7, wherein the accessory protein is a G-protein or a chaperone.

9. The method according to claim 7, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal GPCR.

10. The method according to claim 7, wherein the promotor specific for a sensory neuron is selected from the group comprising *daf-7*, *flp-6*, *gpa-2*, *gpa-4*, *gpa-11*, *gcy-5*, *gcy-6*, *gcy-7*, *gcy-8*, *nhr-38*, *nhr-79*, *odr-7*, *odr-10*, *ops-1*, *str-1*, *str-2*, *str-3*, *sra-7*, *sra-9*, *srg-2*, and *srg-8*.

11. The method according to claim 7, wherein the nematode belongs to the subgenus *Caenorhabditis*.

12. The method according to claim 11, wherein the nematode is *Caenorhabditis elegans*.

13. The method according to claim 7, wherein it is further determined whether the transgenic nematode shows a different behavioral phenotype selected from the group

comprising chemoattraction towards or chemorepulsion from a substance as compared to wild-type nematodes.

14. A transgenic nematode expressing a mammalian GPCR in a sensory neuron linked to behavior.

15. The transgenic nematode according to claim 14, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal GPCR.

16. A transgenic nematode co-expressing a mammalian GPCR and an accessory protein in a sensory neuron linked to behavior.

17. The transgenic nematode according to claim 16, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal GPCR.

18. A method for identifying at least one test substance that is a ligand of at least one mammalian GPCR, said method comprising the steps of

- (a) providing at least one transgenic nematode that expresses at least one mammalian GPCR in sensory neurons linked to behavior;
- (b) contacting said at least one nematode with at least one test substance; and
- (c) detecting modulation of behavior of said at least one nematode in response to said at least one test substance.

19. The method according to claim 18, wherein step (b) comprises placing a medium in a container; placing the at least one test substance on said medium; adding said at least one nematode to said container; and detecting, after a suitable time period, the behavioral response of said at least one nematode over the surface of said medium.

20. The method according to claim 19, wherein the test substance is a water-soluble chemotactic substance and is placed on the medium in a defined zone of the container.

21. The method according to claim 19, wherein the test substance is a volatile chemotactic substance and is placed on the medium at one end of the container.
22. The method according to claim 18, wherein the test substance is provided at at least two different concentrations.
23. The method according to claim 18, wherein the behavior is selected from the group consisting of water-soluble chemoattractive behavior and volatile chemoattractive behavior, and wherein the substance is a chemoattractant substance.
24. The method according to claim 18, wherein the behavior is selected from the group consisting of water-soluble chemorepulsive behavior and volatile chemorepulsive behavior, and wherein the substance is a chemorepulsant substance.
25. The method according to claim 18, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal receptor.
26. The method according to claim 18, wherein the nematode is *C. elegans*.
27. A method of producing a composition comprising the steps of claim 18, modifying the identified substance and formulating the substance obtained with an acceptable carrier or diluent.
28. A method for identifying at least one test substance that is an agonist of a mammalian GPCR, said method comprising the steps of
- (a) providing at least one nematode that expresses at least one mammalian GPCR in sensory neurons that are linked to behavior;
 - (b) contacting said at least one transgenic nematode with the at least one test substance;
 - (c) determining whether said at least one test substance causes an activation of the said behavior in said at least one transgenic nematode; and

- (d) identifying said at least one test substance that causes an activation of said behavior in said at least one transgenic nematode as an agonist of said mammalian GPCR.

29. The method according to claim 28, wherein step (b) comprises placing a medium in a container; placing the at least one test substance on said medium; adding said at least one nematode to said container; and detecting, after a suitable time period, the behavioral response of said at least one nematode over the surface of said medium.

30. The method according to claim 29, wherein the test substance is a water-soluble chemotactic substance and is placed on the medium in a defined zone of the container.

31. The method according to claim 29, wherein the test substance is a volatile chemotactic substance and is placed on the medium at one end of the container.

32. The method according to claim 28, wherein the test substance is provided at at least two different concentrations.

33. The method according to claim 28, wherein the behavior is selected from the group consisting of water-soluble chemoattractive behavior and volatile chemoattractive behavior, and wherein the substance is a chemoattractant substance.

34. The method according to claim 28, wherein the behavior is selected from the group consisting of water-soluble chemorepulsive behavior and volatile chemorepulsive behavior, and wherein the substance is a chemorepulsant substance.

35. The method according to claim 28, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal receptor.

36. The method according to claim 28, wherein the nematode is *C. elegans*.

37. A method of producing a composition comprising the steps of claim 28, modifying the identified substance and formulating the substance obtained with an acceptable carrier or diluent.

38. A method for identifying at least one test substance that is an antagonist of a mammalian GPCR, said method comprising the steps of

- (a) providing at least one nematode that expresses at least one mammalian GPCR in sensory neurons that are linked to behavior, wherein said at least one mammalian GPCR has a known agonist which activates said behavior;
- (b) contacting said at least one transgenic nematode with the at least one test substance in the presence of the known agonist;
- (c) determining whether said at least one test substance causes a suppression of the said behavior in said at least one transgenic nematode; and
- (d) identifying said at least one test substance that causes a suppression of said behavior in said at least one transgenic nematode as an antagonist of said mammalian GPCR.

39. The method according to claim 38, wherein step (b) comprises placing a medium in a container; placing the at least one test substance on said medium; adding said at least one nematode to said container; and detecting, after a suitable time period, the behavioral response of said at least one nematode over the surface of said medium.

40. The method according to claim 39, wherein the test substance is a water-soluble chemotactic substance and is placed on the medium in a defined zone of the container.

41. The method according to claim 39, wherein the test substance is a volatile chemotactic substance and is placed on the medium at one end of the container.

42. The method according to claim 38, wherein the test substance is provided at at least two different concentrations.

43. The method according to claim 38, wherein the behavior is selected from the group consisting of water-soluble chemoattractive behavior and volatile chemoattractive behavior, and wherein the substance is a chemoattractant substance.

44. The method according to claim 38, wherein the behavior is selected from the group consisting of water-soluble chemorepulsive behavior and volatile chemorepulsive behavior, and wherein the substance is a chemorepulsant substance.

45. The method according to claim 38, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal receptor.

46. The method according to claim 38, wherein the nematode is *C. elegans*.

47. A method of producing a composition comprising the steps of claim 38, modifying the identified substance and formulating the substance obtained with an acceptable carrier or diluent.

48. A method for identifying at least one test substance that is a modulator of a mammalian GPCR, said method comprising the steps of

- (a) providing at least one nematode that expresses at least one mammalian GPCR in sensory neurons that are linked to behavior, wherein said at least one mammalian GPCR has a known agonist or antagonist which activates or inhibits said behavior;
- (b) contacting said at least one transgenic nematode with the at least one test substance in the presence of the known agonist or antagonist;
- (c) determining whether said at least one test substance causes a modulation of the said behavior in said at least one transgenic nematode; and
- (d) identifying said at least one test substance that causes a modulation of said behavior in said at least one transgenic nematode as an modulator of said mammalian GPCR.

49. The method according to claim 48, wherein step (b) comprises placing a medium in a container; placing the at least one test substance on said medium; adding said at least one nematode to said container; and detecting, after a suitable time period, the behavioral response of said at least one nematode over the surface of said medium.

50. The method according to claim 49, wherein the test substance is a water-soluble chemotactic substance and is placed on the medium in a defined zone of the container.

51. The method according to claim 49, wherein the test substance is a volatile chemotactic substance and is placed on the medium at one end of the container.

52. The method according to claim 48, wherein the test substance is provided at at least two different concentrations.

53. The method according to claim 48, wherein the behavior is selected from the group consisting of water-soluble chemoattractive behavior and volatile chemoattractive behavior, and wherein the substance is a chemoattractant substance.

54. The method according to claim 48, wherein the behavior is selected from the group consisting of water-soluble chemorepulsive behavior and volatile chemorepulsive behavior, and wherein the substance is a chemorepulsant substance.

55. The method according to claim 48, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal receptor.

56. The method according to claim 48, wherein the nematode is *C. elegans*.

57. A method of producing a composition comprising the steps of claim 48, modifying the identified substance and formulating the substance obtained with an acceptable carrier or diluent.

58. A method for evaluating the potency of mammalian GPCR activation by a known ligand, said method comprising the steps of

- (a) providing at least one nematode that expresses at least one mammalian GPCR in sensory neurons that are linked to behavior, wherein said at least one mammalian GPCR has a known ligand;
- (b) contacting said at least one nematode with said ligand and at least one structurally related substance; and

- (c) detecting the behavioral response of said at least one nematode to said at least one structurally related substance; and
- (d) comparing the behavioral response of said at least one nematode to said ligand to the behavioral response of said at least one nematode to said at least one structurally related substance.

59. The method according to claim 58, wherein the mammalian GPCR is a mammalian taste, olfactory or vomeronasal receptor.

60. The method according to claim 58, wherein the nematode is *C. elegans*.

61. A method of producing a composition comprising the steps of claim 58, modifying the identified substance and formulating the substance obtained with an acceptable carrier or diluent.